Complete Summary

GUIDELINE TITLE

Standards for breast conservation therapy in the management of invasive breast carcinoma.

BIBLIOGRAPHIC SOURCE(S)

Standards for breast conservation therapy in the management of invasive breast carcinoma. CA Cancer J Clin 2002 Sep-Oct;52(5):277-300. [82 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Invasive breast carcinoma

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management

CLINICAL SPECIALTY

Oncology
Pathology
Radiation Oncology
Radiology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To provide standards for diagnosis and management of invasive breast carcinoma
- To update the 1997 recommendations issued by the American College of Radiology on the diagnosis and management of invasive breast carcinoma [CA Cancer J Clin 1998 Mar-Apr;48(2):83-107]

TARGET POPULATION

Patients with invasive breast cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis and Evaluation

1. History and Physical Examination
2. Mammographic Evaluation
3. Pathologic Evaluation
4. Patient Preferences

Treatment

1. Pre-operative Chemotherapy
2. Breast Conservation Surgery
3. Radiation Therapy
4. Follow-up Care

MAJOR OUTCOMES CONSIDERED

- Breast cancer mortality
- Efficacy of treatment (breast conservation surgery with radiation or mastectomy) as measured by overall and disease-free survival at 10 years
- Risk of recurrence following breast conservation surgery and radiation or mastectomy
- Psychological outcomes following surgery including global measures of emotional distress and quality of life
- Cosmetic outcomes following breast-conservation surgery or reconstructive surgery

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE is the principle database used for search of peer-reviewed journals for articles related to the standard.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Each standard, representing a policy statement by the American College of Radiology, has undergone a thorough consensus process in which it has been subject to extensive review.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The Standard was approved by the American College of Radiology, the American College of Surgeons, the Society of Surgical Oncology, and the College of American Pathologists.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Patient Selection and Evaluation

Because of the potential options for treatment of early-stage breast cancer, careful patient selection and a multidisciplinary approach are necessary. Four critical elements in patient selection for breast-conservation treatment are history and physical examination, mammographic evaluation, histologic assessment of the resected breast specimen, and assessment of the patient's needs and expectations.

History and Physical Examination

Much of the information needed to determine a patient's suitability for breast conservation therapy can be obtained from a detailed history and physical examination. It is important to note that age per se, whether young or old, is not a contraindication to breast conservation. In the elderly, physiologic age and the presence of comorbid conditions should be the primary determinants of local therapy. The elements of the breast history and physical exam are listed in Tables 8 and 9 in the original guideline document. When evaluating the physical examination, it is important to note that skin, nipple, and breast parenchyma retraction are not signs of locally advanced breast cancer and do not represent contraindications to breast conservation.

Mammographic Evaluation

Recent preoperative mammographic evaluation is necessary to determine a patient's eligibility for breast conservation treatment. It should be done with high-quality, dedicated mammographic equipment in a facility certified by the U.S. Food and Drug Administration (FDA) under the Mammography Quality Standards Act.

Recent (usually within 3 months) mammographic evaluation, before biopsy or definitive surgery, plays an important role in establishing the appropriateness of breast-conservation treatment by defining the extent of a patient's disease, the presence or absence of multicentricity, and other factors that might influence the treatment decision. It is important for evaluating the contralateral breast. Bilateral mammography is required for palpable lesions as well as nonpalpable lesions that can be identified only radiographically. Nonpalpable masses and microcalcifications comprise an increasing percentage of carcinomas treated with breast conservation.

The breast tumor should be measured in at least two dimensions on the mammographic views or from the sonogram during ultrasonography, if it is performed. The size of the tumor should be included in the mammographic report.

If the tumor is a poorly marginated mass, approximate dimensions can be given from either the mammogram or the sonogram. The skin of the breast in the area of a mass should be evaluated for thickening that might signify tumor involvement. If the mass is associated with microcalcifications, an assessment of the extent of the calcifications within and outside the mass should be made, including the dimensions of the area in which calcifications are located. If one or more clusters of microcalcifications are the only markers of the tumor, their location and distribution should be described. For evaluation of masses and microcalcifications, specialized views with positioning adapted to the location of the abnormality may be helpful. Magnification mammography and spot compression are important for characterizing microcalcifications and defining the margins of masses. Ipsilateral multifocality or multicentricity may be present and influence the treatment selection. In every instance, when one abnormality is seen, all areas of each breast should be fully evaluated for the presence of additional disease.

Some studies have suggested that magnetic resonance (MR) imaging is a useful adjunct to mammography and ultrasound for the identification of multifocal and multicentric disease. At this time, due to the lack of standardization of technique, high false positive rates, and difficulty in biopsying lesions only seen on MRI, this cannot be considered part of the standard evaluation of the breast cancer patient. Using magnification mammography and ultrasound, patients with tumors suitable for breast conservation can be identified with at least 95% certainty preoperatively.

Pathologic Features Influencing Treatment Choice

A number of pathologic factors have been assessed for their ability to predict an increased risk of recurrence in the treated breast in patients undergoing conservative surgery and radiation. These factors include histologic type and grade, the presence or absence of tumor necrosis, vascular or lymphatic invasion or an inflammatory infiltrate, the presence of ductal carcinoma in situ (DCIS) in association with an invasive ductal carcinoma, margins of resection, and the pathologic nodal status. A discussion of these factors can be found in the original guideline document.

Pathologic Evaluation

The excised tissue should be submitted for pathology examination with appropriate clinical history and anatomic site specifications, including laterality (right or left breast) and quadrant. For wide excisions or segmental breast resections, the surgeon should orient the specimen (e.g., superior, medial, lateral) for the pathologist with sutures or other markers. Gross examination should document the type of surgical specimen (e.g., excisional biopsy, quadrantectomy), the size of the specimen, the measured size of the tumor, and the proximity of the tumor or biopsy site to the margins of excision. The presence or absence of tumor at the margins of excision is determined by marking them with India ink or another suitable technique.

Frozen section preparation of tissue obtained from image-guided needle biopsies of nonpalpable lesions or tumors less than 1-cm is strongly discouraged. Small foci of invasive carcinoma or microinvasive disease may be lost or rendered

uninterpretable by freezing artifact. In general, frozen sections should be prepared only when there is sufficient tissue that the final diagnosis will not be compromised and when the information is necessary for immediate therapeutic decisions.

The use of compression devices for specimen radiography may be necessary to visualize the lesion in the specimen. However, these devices may result in falsely close margins, particularly in specimens consisting predominately of fat. This is due to the compressibility of fat relative to the tumor, rather than to any alteration of the tumor.

The pathologist includes certain basic data in each surgical pathology consultation report because they are of prognostic importance or are needed for staging or therapy.

Features that should be included in the surgical pathology consultation report for invasive carcinoma include:

- How the specimen was received (e.g., number of pieces, fixative, orientation)
- The laterality and quadrant of the excised tissue and the type of procedure, as specified by the surgeon
- The measured size of the tumor (in three dimensions if possible), with verification by microscopic examination, particularly for pT1 lesions or those associated with an extensive intraductal component (EIC)
- Histologic type and grade
- The presence or absence of coexistent ductal carcinoma in situ or an extensive intraductal component
- The presence or absence of peritumoral vascular or lymphatic invasion
- The presence or absence of gross or microscopic carcinoma (either invasive carcinoma or ductal carcinoma in situ) at the margins of excision. If tumor is not at the margin, the distance of the tumor or biopsy site from the margin should be stated
- The presence and location of microcalcifications
- Lymph node status. This should be recorded as the number of lymph nodes found in the specimen and the number of involved nodes, the size of the largest involved node, and the presence or absence of extension beyond the lymph node capsule.

The presence of a focus of tumor measuring 2 mm or less within a lymph node identified by routine histologic examination is defined as a micrometastasis and is classified as pN1a. The clinical significance of multiple micrometastatic foci is unknown; however, it is recommended that they also be classified as pN1a until further information becomes available.

The significance of individual cells or isolated cellular groups found exclusively by immunohistochemistry, either in a lymph node removed by a routine lymph node dissection or in a sentinel node, is unclear. The College of American Pathologists currently recommends that these be classified as pN0.

It is important to specify the presence of any special histologic type of invasive breast cancer (e.g., tubular, mucinous, papillary), most of which are considered low grade. All ordinary invasive carcinomas (ductal, not otherwise specified)

should be assigned a histologic grade; some authors recommend grading invasive lobular carcinoma as well. If a specific grading system is used, this should be stated in the pathology report. The most commonly used histologic grading system is the Elston modification of the Bloom-Richardson scheme. This system evaluates degree of tubule formation, nuclear grade, and mitotic rate to determine an overall histologic score.

The assessment of surgical margins is arguably the most important aspect in the pathologic evaluation of breast tumor excision in patients being considered for breast conservation. Although the definitions of "positive" and "negative" margins vary among institutions, microscopic margin involvement appears to be associated with an increased risk of local recurrence and, in most cases, indicates a need for further surgery, such as re-excision of the tumor site.

Microscopic confirmation of the presence or absence of regional or distant metastasis must be confirmed microscopically when appropriate tissue is submitted for examination. The AJCC/UICC (American Joint Committee on Cancer/International Union Against Cancer) pTNM (T-primary tumor; N-regional nodes; M-metastasis) classification is recommended for appropriate stage grouping.

Determination of estrogen and progesterone receptors is standard for invasive breast carcinomas. This can be done either by the traditional ligand-binding assays performed on snap frozen tissue or by immunohistochemistry performed on routinely fixed tissue sections. The results of ancillary studies (such as steroid receptor analysis, DNA ploidy, proliferative rate, etc.) are usually reported in an addendum or supplement to the surgical pathology report.

Patient Preferences

Perhaps the most difficult aspect of patient evaluation is the assessment of the patient's needs and expectations regarding breast preservation. The patient and her physician must discuss the benefits and risks of mastectomy compared to breast conservation treatment in her individual case with thoughtful consideration of each. Each woman must evaluate how her choice of treatment is likely to affect her sense of disease control, self-esteem, sexuality, physical functioning, and overall quality of life. A number of factors should be considered:

1. Long-term survival
2. The possibility and consequences of local recurrence
3. Psychological adjustment (including the fear of cancer recurrence), cosmetic outcome, sexual adaptation, and functional competence

For most patients, the choice of mastectomy with or without reconstruction or breast-conservation treatment does not influence the likelihood of survival, but it may have a differential effect on the quality of life. Psychological research comparing patient adaptation following mastectomy and breast conservation treatment shows no significant differences in global measures of emotional distress. Research also does not reveal significant changes in sexual behavior and erotic feelings in the treated breast or nipple and areolar complex. However, women whose breasts are preserved have more positive attitudes about their

body image and experience fewer changes in their frequency of breast stimulation and feelings of sexual desirability.

Absolute and Relative Contraindications

In the selection of patients for breast conservation treatment with radiation, there are some absolute and relative contraindications:

Absolute contraindications

a. Pregnancy is an absolute contraindication to the use of breast irradiation. However, in many cases, it may be possible to perform breast conserving surgery in the third trimester and treat the patient with irradiation after delivery.
b. Women with two or more primary tumors in separate quadrants of the breast or with diffuse malignant-appearing microcalcifications are not considered candidates for breast conservation treatment.
c. A history of prior therapeutic irradiation to the breast region that would require retreatment to an excessively high total radiation dose to a significant volume is another absolute contraindication.
d. Persistent positive margins after reasonable surgical attempts. The importance of a single focally positive microscopic margin needs further study and may not be an absolute contraindication.

Relative contraindications

a. A history of collagen vascular disease is a relative contraindication to breast conservation treatment because published reports indicated that such patients tolerate irradiation poorly. Most radiation oncologists will not treat patients with scleroderma or active lupus erythematosus, considering it an absolute contraindication. In contrast, rheumatoid arthritis is not a relative or absolute contraindication.
b. The presence of multiple gross tumors in the same quadrant and indeterminate calcifications must be carefully assessed for suitability because studies in this area are not definitive.
c. Tumor size is not an absolute contraindication to breast conservation treatment, although there is little published experience in treating patients with tumor sizes greater than four to five centimeters. However, a relative contraindication is the presence of a large tumor in a small breast in which an adequate resection would result in significant cosmetic alteration. In this circumstance, preoperative chemotherapy should be considered.
d. Breast size can be a relative contraindication. Treatment by irradiation of women with large or pendulous breasts is feasible if reproducibility of patient set-up can be assured and the technical capability exists for greater than or equal to 6 MV photon beam irradiation to obtain adequate dose homogeneity.

Nonmitigating Factors

There are certain clinical and pathologic features that should not prevent patients from being candidates for breast conservation treatment. These features include the presence of clinically suspicious and mobile axillary lymph nodes or microscopic tumor involvement in axillary nodes. In addition, it is important to

emphasize that it is feasible to evaluate the breast for local recurrence. The changes associated with recurrence can be detected at an early stage through the use of physical examination and mammography. The delivery of irradiation in this setting does not result in a meaningful risk of second tumors in the treated area or in the untreated breast.

Tumor location is not a factor in the choice of treatment. Tumors in a superficial subareolar location may occasionally require the resection of the nipple/areolar complex to achieve negative margins, but this does not impact on outcome. Whether this is preferable to mastectomy needs to be assessed by the patient and her physician.

Family History

A family history of breast cancer is not a contraindication to breast conservation. Several studies have shown that the rate of breast recurrence in patients with first- or second-degree relatives with breast cancer does not differ from than that seen in patients without a family history of breast cancer. In patients with genetic breast cancer, it is not clear that the risk of ipsilateral breast tumor recurrence is increased. However, these patients appear to be at a substantially increased risk of new primary breast cancers in both the ipsilateral and contralateral breast over time, and this should be considered during the treatment counseling process. A high risk of systemic relapse is not a contraindication for breast conservation, but a determinant of the need for adjuvant therapy.

Preoperative Chemotherapy

Patients who are not candidates for breast conservation on the basis of a large tumor in a small breast should be considered for preoperative chemotherapy to reduce the tumor size. This approach is not appropriate for patients with evidence of multicentricity on the initial mammogram. The National Surgical Adjuvant Breast and Bowel Project (NSABP) has reported the results of a large randomized trial in which 1,523 patients with T1-3 N0-1 breast cancer were randomized to surgery followed by 4 cycles of adriamycin cytoxin (AC) or adriamycin cytoxin before surgery. At 5 years of follow-up, no differences in disease-free or overall survival were seen. Breast conservation was able to be performed in 67.8% of patients having preoperative chemotherapy versus 59.8% having initial surgery ($p=0.003$). Overall, no difference was seen in the incidence of breast recurrence between the preoperative (7.9%) and the postoperative (5.8%) group. However, among patients able to undergo lumpectomy only after downstaging by chemotherapy, the local failure rate was 14.5%, compared to 6.9% in those believed to be candidates for breast conservation before chemotherapy ($p=0.04$). The increased risk was observed regardless of patient age or tumor size, and it emphasizes the need for careful attention to evaluation of the extent of disease and the technical details of resection in these patients. Percutaneous placement of tumor marker clips within the primary tumor is recommended for tumors less than 5-cm in size to provide a landmark for localization and excision should a clinical and radiographic complete response to chemotherapy occur.

Technical Aspects of Surgical Treatment

When breast-conservation treatment is appropriate, the goals of any surgical procedure on the breast are total gross removal of the suspicious or known malignant tissue with minimal cosmetic deformity. These goals apply to either diagnostic biopsy or definitive local excision before radiation therapy. Failure to consider these goals at all stages may jeopardize conservation of the breast.

In most cases, local anesthesia can be used for the biopsy. Frequently, local anesthesia also can be used for the definitive local excision, particularly when it is combined with intravenous sedation in selected patients.

Skin Incision

The placement and performance of the skin incision can be critical to the quality of cosmesis. Curvilinear skin incisions following Langer's lines generally achieve the best cosmetic result. However, at the 3 o´clock and 9 o´clock positions and in the lower breast, a radial incision may provide a better result, particularly if skin removal is necessary.

The incision should be over or close to the tumor and of adequate size to allow the tumor to be removed in one piece. In the upper inner aspect of the breast, some retraction of the skin may be necessary to avoid an incision that may be visible with clothing. Periareolar incisions for lesions in the periphery of the breast are inappropriate.

Excision of a segment of skin rarely is necessary and is undesirable because it may alter the position of the nipple or the inframammary crease. Preservation of the subcutaneous tissue with separate closure improves the cosmetic result. The skin should be closed with a subcuticular technique.

Breast Tissue Management

The primary lesion should be excised with a rim of grossly normal tissue, avoiding excessive sacrifice of breast tissue. Very superficial tumors in the subareolar area may require excision of the nipple-areolar complex to assure adequate tumor margins and to avoid devascularization. (Partial areolar excision with careful approximation for small lesions in the immediate subareolar area can provide adequate tissue removal and good cosmesis.) Closure of the breast tissue may reduce the occurrence of a saucer-like defect, but the overall cosmetic result with nipple-areolar sacrifice is less than optimal.

Lesions within the substance of the breast should be approached by incising the overlying breast tissue. A superior cosmetic effect is usually achieved when the breast is not reapproximated. Reapproximation that appears to be adequate with the patient relaxed and supine often results in distortion of the breast when the patient is upright and mobile.

Meticulous hemostasis is of critical importance. Hematoma formation produces changes that are difficult to interpret by physical examination. In addition, the evolving scar from a hematoma makes mammography interpretation difficult. These changes may be long-lasting and lead to unnecessary biopsy because of the difficulty in evaluation.

Drains in the breast should be avoided.

Specimen orientation by the surgeon with the use of sutures, clips, multicolored indelible ink, or another suitable technique is important. The specimen should not be sectioned before it is submitted to the pathologist. The surgeon should examine the specimen for the determination of a grossly clear margin. If a clear margin is not evident, re-excision should be performed at that time. Routine frozen section evaluation of margins is optional and does not guarantee negative margins after a complete examination. Any uncertainty regarding orientation of the specimen should be clarified for the pathologist by the surgeon. In addition, clips outlining the breast defect may aid the planning and execution of radiation therapy and demarcate the tumor bed for future imaging studies.

Image-Directed Surgery

Nonpalpable carcinoma may be diagnosed by image-directed biopsy or needle localization and excision. If a patient has a nonpalpable carcinoma diagnosed by image-guided biopsy, then breast-conserving surgery should be conducted with presurgical localization with a guide such as guide wire. This will be facilitated by the placement of a marker clip when image-guided biopsy is done for small lesions, which are likely to be completely removed by the procedure.

Suspicious lesions detected by mammography require presurgical localization in order to assure accurate removal of the abnormal area and to avoid excess sacrifice of breast tissue. The method of localization may be needle-hook wire, blue dye injection, or a combination of both. The localization should be precise. Labeled craniocaudal and lateral films that show the hookwire should be sent to the operating room for the surgeon's orientation. The surgeon usually should assess the exact location by triangulation based on the position, depth of penetration, and angle of the wire and place the incision closest to the tip of the wire to achieve the best cosmetic result. Tunneling should be avoided, and the surgeon should attempt to make the skin incision as close to the lesion as possible. The same principles of skin incision and breast tissue management used for palpable cancers should be employed.

Localization titanium clips may be left in the excision cavity to aid in placement of irradiation boost volume and to ensure adequate coverage with tangential fields, especially for lateral and medial lesions.

Specimen Radiograph

A radiograph of the specimen should be obtained, preferably in two dimensions (orthogonal projections). Magnification and compression of the specimen increase the resolution of the radiograph. The specimen film should be correlated with a preoperative mammogram and interpreted without delay. The radiologist's report should indicate whether the mammographic abnormality (mass or calcifications) is seen in the specimen and if it has been removed completely, as far as can be determined. The proximity of the abnormality to the edge of the resected tissue should be noted. The radiologist should communicate these findings to the surgeon in the operating room before the excision site is closed so that additional tissue can be removed if necessary. Subsequent specimens also should be radiographed. Specimen radiography may be useful in confirming removal of

masses that are palpable intraoperatively to ensure that they correspond to the mass lesion seen mammographically.

Re-excision of Biopsy Site

Re-excision of the previous biopsy site to assure negative margins of resection must be carefully performed in order to accomplish this goal, avoid excess breast tissue removal, and achieve good cosmesis. Proper orientation of the original biopsy specimen (for example, short suture in the superior margin, long suture in the lateral margin) will allow identification of the individual margin surfaces involved with tumor. Re-excision can be limited to those areas. When the specimen has not been oriented, removal of a rim of tissue around the entire previous biopsy is necessary.

For larger biopsy cavities, shaving of each individual margin and marking of the new margin surface with sutures, clips, or ink allows removal of residual tumor with preservation of a maximum amount of breast tissue. For very small cavities, removal of the entire biopsy site as an en bloc specimen is acceptable.

Special Considerations in Patients Receiving Preoperative Chemotherapy

Additional breast imaging studies should be obtained following the planned course of chemotherapy to assess the patient´s suitability for breast-conserving therapy. However mammography does not reliably exclude persistent microscopic tumor, and architectural distortions and calcification do not always indicate residual disease. Breast MRI may be a more accurate method of assessing the extent of residual invasive tumor when expertise with this technique is available.

The initial surgical resection in these patients should include the removal of any clinically or radiographically abnormal tissue. If viable tumor is present throughout the specimen even if it does not extend to the margin, a further re-excision should be considered. If additional viable tumor is present in the re-excised specimen, a re-evaluation of the patient´s suitability for breast conservation is necessary.

Management of the Axillary Nodes

Axillary dissection is the standard technique for management of the axillary nodes. A level I and II axillary dissection will provide accurate staging information and maintain local control in the axilla. In the patient undergoing mastectomy, axillary dissection should be performed through the mastectomy ellipse. In the patient undergoing breast conservation, the breast incision and the axillary incision should be separate. A continuous incision from the breast to the axilla results in unnecessary deformity. Occasionally, a tumor in the axillary tail can be removed through the same incision used to remove the axillary nodes. A transverse incision in the low axilla from just posterior to the border of the pectoralis major to nearly the anterior border of the latissimus dorsi obtains an excellent cosmetic result and excellent exposure. Some surgeons prefer a vertical incision posterior and parallel to the border of the pectoralis major, which also provides good exposure and cosmetically good results. During dissection, the long thoracic nerve, the thoraco dorsal nerve, and the medial pectal nerve should be preserved. Preservation of the intercostal brachio-cutaneous nerve is desirable, as

numbness of the posterior upper arm is less likely to occur with nerve preservation. At times, preservation of this nerve should not be performed because of grossly involved lymph nodes. Stripping of the axillary vein is unnecessary and should be condemned because it increases the incidence of lymphedema. Usually, closed suction drainage is advisable.

Recently, an alternative to axillary dissection, a sentinel node biopsy or sentinel lymph node dissection, has become popular. This procedure has been extremely successful at a number of major institutions. However, its widespread applicability remains to be determined, and long-term follow-up on a significant number of women undergoing sentinel node biopsy alone is lacking. For these reasons, the technique should be considered investigational at most centers. Lymphatic mapping for sentinel lymph node dissection can be accomplished with 1% isosulfan blue dye or radiolabeled colloids. Usually, a combination of technetium sulfur colloid and dye is used.

Sentinel node dissection is indicated for small primary tumors with clinically negative axillary lymph nodes and no prior axillary surgery. Pregnancy or multicentric carcinomas are contraindications. Prior augmentation mammoplasty, extensive surgical biopsy, and prior reduction mammoplasty may be relative contraindications.

Experience with the technique after neoadjuvant chemotherapy is limited, and the available studies suggest a high false-negative rate. Sentinel node dissection in this circumstance should be considered investigational and be performed only under investigational protocols.

For patients who require preoperative chemotherapy, sentinel node biopsy can be performed prior to the initiation of chemotherapy. In general, patients with metastases in sentinel nodes detected by hematoxylin and eosin should undergo complete Level I and II axillary dissection. Immunohistochemistry should not be routinely performed, as the significance of metastases in sentinel nodes detected only by immunohistochemistry remains to be determined. Therapeutic decisions should be made on the basis of metastases identified by hematoxylin and eosin staining.

In experienced hands, this sentinel node dissection has been shown to be extremely accurate in predicting axillary status and is likely to replace axillary lymph node dissection for women with tumor free sentinel nodes. Experience with this technique prior to abandoning axillary lymph node dissection is essential. Surgeons should perform both sentinel node biopsy and axillary lymph node dissection until they are confident that the procedure can be performed with identification of sentinel nodes in at least 90% of patients with a false-negative rate of 10% or less. For most surgeons, this requires 20-30 sentinel node biopsies followed by axillary dissections to determine an individual surgeon´s technical accuracy. Level I and II axillary lymph node dissection should be performed as standard therapy.

Sentinel node biopsy usually results in minimal morbidity; however, rehabilitation after axillary lymph node dissection or sentinel node biopsy is essential. Usually, patients after sentinel node biopsy require no formal exercise to return to full function. Patients after axillary dissection should be given formal exercise training

to prevent a frozen shoulder. Use of shoulder immobilization and arm slings or wraps should be avoided, as these contribute to a frozen shoulder. If a patient does not achieve early recovery or full shoulder function (by 6-8 weeks), physical therapy should be instituted to avoid permanent dysfunction.

Techniques of Irradiation

A multidisciplinary approach is necessary for optimal breast-conservation treatment. Radiation therapy should be delivered only after evaluation of the mammography findings, the pathology findings, and the surgical procedures performed on the patient. The optimal combination of surgery and irradiation to achieve the dual objectives of local tumor control and preservation of cosmetic appearance varies from patient to patient. The optimal combination is determined by the extent, nature, and location of the tumor; the patient's breast size; and the patient's relative concerns about local recurrence and preservation of cosmetic appearance. Close cooperation between radiation oncologists and medical oncologists also is important because irradiation and adjuvant chemotherapy require integration if both treatment modalities are used. Elements in the technique of irradiation and techniques to avoid are presented in the original guideline document.

Follow-up Care

Follow-up assessment of the results of breast conservation treatment emphasizes the cosmetic outcome and the functional consequences. Regular follow-up examination includes the following goals:

1. Early detection of recurrent or new cancer, allowing timely intervention
2. Identification of any treatment sequelae and appropriate interventions when indicated
3. Providing the individual practice with the database necessary to optimize treatment and compare outcomes with national standards

Regular history and physical examination in conjunction with breast imaging are the cornerstones of effective follow-up care. Unfortunately, many patients perceive history and physical examination to be less important as reliable follow-up measures than sophisticated medical testing. A public education effort is needed to address this problem.

The following evaluations should be performed by the physician at cited intervals following the completion of treatment:

Examinations and Mammography

History and physical examination

Local failure occurs at a constant rate from years 2 through 8 post-treatment; therefore, examination frequency should be based on risk factors for both local and distant recurrence.

Examination frequency:

Every 3 to 6 months, years 1 to 3. This will vary for patients receiving adjuvant chemotherapy, who need more frequent assessment during the course of their active treatment.

Every 6 months, years 4 and 5. Some investigators prefer to continue semiannual examinations through year 8 because the rate of local recurrence is constant through that time interval.

Annually after year 5. More frequent follow-up for patients at exceptionally high risk may be needed.

Mammography

A goal of follow-up imaging of the treated breast is the early recognition of tumor recurrence. To prevent unnecessary biopsy, it is important to know that postoperative and irradiation changes overlap with signs of malignancy on a mammogram. The changes include masses (postoperative fluid collections and scarring), edema, skin thickening, and calcifications.

At times, these changes may be impossible to distinguish. Postsurgical and radiation edema, skin thickening, and postoperative fluid collections are most marked in the first 6 months. After the first 6 to 12 months, radiographic changes slowly resolve, and demonstrate stability within 2 years for most patients.

In order to interpret mammograms accurately and assess the direction of change, the current mammogram must be compared in sequence with preceding studies. The diagnostic radiologist can tailor mammographic studies of the treated breast to the surgical site by using special mammographic views in addition to routine mediolateral oblique and craniocaudal views. Magnification and spot compression can be used with any view to increase detailed visualization of the site of tumor excision and other areas. Magnification mammography is useful to classify calcifications morphologically and to quantitate them. In some cases, a view with the x-ray beam tangential to the scar and various other additional obliquities will be helpful to differentiate recurrent tumor from postprocedural changes.

Ultrasonography can characterize a postoperative mass, such as a seroma, as fluid filled rather than solid. As these masses resolve and scars form, a spiculated soft tissue density that mimics tumor may be seen on the mammogram. Additional radiographic projections of the site of tumor removal facilitate more confident radiographic interpretations.

<u>Schedule of Imaging of the Treated Breast</u>

1. Postoperative, preradiation therapy mammography is particularly important after malignant microcalcifications have been removed or if the adequacy of the resection is questioned. Magnification mammography can be useful in identifying or verifying possible residual malignant calcifications.
2. A baseline mammogram for comparison should be performed 6 to 9 months after tumor excision and completion of all therapies.
3. At least annually thereafter, or at more frequent intervals as warranted by clinical or radiographic findings.

Schedule of Imaging of the Contralateral Breast

Mammography should be performed annually, according to the guidelines endorsed by both the American College of Radiology and the American Cancer Society and with synchronization of surveillance mammography of the treated breast. More frequent intervals may be warranted by clinical or radiographic findings. (The risk of cancer is approximately the same for both the treated and the untreated breast.)

Other Tests

Symptomatic patients are justifiably evaluated with other medical tests (e.g., radionuclide bone scan, chest radiography, computerized tomography [CT] scans, liver function tests) as indicated by the character of their medical problem. An annual chest radiograph in patients who smoke may be appropriate. Randomized controlled trials have shown that routine use of these tests provides no benefit for asymptomatic patients with Stage I or II breast carcinoma. No survival benefits have been shown, and the cost-effectiveness of using such procedures in routine follow-up is seriously in question. (See American College or Radiology [ACR] Appropriateness Criteria, Vol. 2, Imaging Workup for Stage I Breast Carcinoma, 1996).

Evaluation of Sequelae

At the time of the first follow-up examination, and serially thereafter, the physician should evaluate the patient for any treatment-related toxicities. This evaluation should include the following:

1. Assessment of the overall cosmetic result. A 4-point scoring system is recommended for assessing the cosmetic result. (See Appendix A in the original guideline document.)
2. Assessment of complications. Complications should be specified with regard to symptomatology and physical findings. The use of the RTOG/EORTC (Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer) Radiation Toxicity Scoring Scheme is recommended for the grading of complications. In addition, the simple measurement of arm circumference at fixed distances above and below the olecranon is recommended for the evaluation and quantification of arm edema.
3. Patient evaluation of results. The patient's evaluation of treatment outcomes in terms of psychological, functional, and cosmetic consequences should be taken into account in the follow-up process.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Six modern prospective randomized trials have compared mastectomy with conservative surgery and radiation for stage I and II breast cancer. A published meta-analysis included nine prospective randomized trials comparing conservative surgery and radiation with mastectomy. 10 randomized trials have compared conservative surgery alone to conservative surgery and radiation. The results of multiple, nonrandomized retrospective studies were also evaluated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

General

- Effective multidisciplinary diagnosis and management of invasive breast carcinoma
- Appropriate selection of patients for breast conservative surgery

Benefits of Breast-Conservation Surgery Compared to Mastectomy

The results of prospective randomized trials and the results of large retrospective nonrandomized studies from single institutions have shown that breast-conservation treatment and mastectomy are equally effective for appropriately selected patients with early-stage breast cancer. Both treatment options are associated with overall survival rates of 60-80% and disease-free survival rates of 50-70%, reported at 6-18 years follow-up. Local recurrence rates following either treatment regimen range from 3-20%.

Benefits of Breast-Conservation Surgery with Radiation versus without Radiation

A recent meta-analysis of 10 randomized trials comparing conservative surgery to conservative surgery and radiation reported an absolute reduction in breast recurrence rates with radiation of 17% for axillary-node-negative women (25% versus 7.8%) and 19% for axillary-node-positive women (35.4% versus 16.1%). The absolute benefit from radiation for any recurrence was 16% for the node-negative group (44.7% versus 28.6%, p=<0.00001) and 8% for the node-positive group (58% versus 49.8%, p=0.002). In another study which randomized women with primary tumors of less than 2 cm, histologic grade 1, and negative axillary nodes to wide excision and radiation with or without tamoxifen, the ipsilateral breast tumor recurrence rate was 5% in the patients who did not receive radiation and 2% in those who received radiation (with a median follow-up of 4 years). Radiation, therefore, appears to benefit all women with early-stage invasive breast cancer, although the magnitude of this benefit varies depending on the selection of the patients.

Subgroups Most Likely to Benefit:

Women with early-stage invasive breast cancer appear to benefit from breast conserving surgery and radiation therapy.

POTENTIAL HARMS

Not stated

CONTRAINDICATIONS

CONTRAINDICATIONS

Absolute and Relative Contraindications

Some absolute and relative contraindications exist in the selection of patients for breast conservation treatment with radiation.

Absolute Contraindications

- Pregnancy is an absolute contraindication to the use of breast irradiation. However, in many cases, it may be possible to perform breast conserving surgery in the third trimester and treat the patient with irradiation after delivery.
- Women with two or more primary tumors in separate quadrants of the breast or with diffuse malignant-appearing microcalcifications are not considered candidates for breast conservation treatment.
- A history of previous therapeutic irradiation to the breast region that would require retreatment to an excessively high total radiation dose to a significant volume is another absolute contraindication.
- Finally, persistent positive margins after reasonable surgical attempts absolutely contraindicate breast conservation treatment with radiation. The importance of a single focally positive microscopic margin needs further study and may not be an absolute contraindication.

Relative Contraindications

- A history of collagen vascular disease is a relative contraindication to breast conservation treatment because published reports indicate that such patients tolerate irradiation poorly. Most radiation oncologists will not treat patients with scleroderma or active lupus erythematosus, considering either an absolute contraindication. In contrast, rheumatoid arthritis is not a relative or an absolute contraindication.
- The presence of multiple gross tumors in the same quadrant and indeterminate calcifications must be carefully assessed for suitability because studies in this area are not definitive.
- Tumor size is not an absolute contraindication to breast conservation treatment, although there is little published experience in treating patients with tumor sizes greater than 4 to 5 cm. However, a relative contraindication is the presence of a large tumor in a small breast in which an adequate resection would result in significant cosmetic alteration. In this circumstance, preoperative chemotherapy should be considered.
- Breast size can be a relative contraindication. Treatment by irradiation of women with large or pendulous breasts is feasible if reproducibility of patient set-up can be ensured and the technical capacity exists for greater than or equal to 6-MV photon beam irradiation to obtain adequate dose homogeneity.

QUALIFYING STATEMENTS

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The standards of the American College of Radiology (ACR) are not rules but are guidelines that attempt to define principles of practice that should generally produce high-quality radiological care. The physician and medical physicist may modify an existing standard as determined by the individual patient and available resources. Adherence to American College of Radiology standards will not ensure a successful outcome in every situation. The standards should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The standards are not intended to establish a legal standard of care or conduct, and deviation from a standard does not, in and of itself, indicate or imply that such medical practice is below an acceptable level of care. The ultimate judgment regarding the propriety of any specific procedure or course of conduct must be made by the physician and medical physicist in light of all circumstances presented by the individual situation.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The Standards that are approved at each Annual Meeting are distributed to the membership by a separate mailing for implementation in their practices. All American College of Radiology (ACR) Standards are also available to members and the general public on the College´s Web site: www.acr.org.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Standards for breast conservation therapy in the management of invasive breast carcinoma. CA Cancer J Clin 2002 Sep-Oct;52(5):277-300. [82 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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American College of Radiology; American College of Surgeons; College of American Pathologists; Society of Surgical Oncology

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

American College of Radiology Members: Eric A. Strom, MD (Co-Chair); Lawrence W. Bassett, MD; Barbara L. Fowble, MD; Jay R. Harris, MD

American College of Surgeons Members: Monica Morrow, MD (Co-Chair, Senior Editor); Armando Giuliano, MD; S. Eva Singletary, MD; David P. Winchester, MD

College of American Pathologists Members: Frances O´Malley, MD; Stuart J. Schnitt, MD

American College of Radiology Staff: John Curry; Marie Zinninger; Sandra Bjork

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

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ENDORSER(S)

American College of Surgeons - Medical Specialty Society
College of American Pathologists - Medical Specialty Society
Society of Surgical Oncology - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previously released version (CA Cancer J Clin 1998 Mar-Apr;48[2]:83-1).

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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